Remarks

Claims 82-132 are pending. Claims 82, 91, 97, 109, 116, 121 and 128 have been amended. Claim 133 has been canceled. **Claims 1-81 were previously canceled.** Claims 82, 91, 97, 109, 116, 121 and 128 have now been amended to include all of the limitations of claims deemed to be allowable if written in independent form.

The claimed invention is based upon the discovery that PHA production can be targeted to peroxisomes, where there is a great concentration of substrate for production of the polymers, by targeting the enzymes required for production of the PHAs to the peroxisomes. This is achieved by construction of fusion nucleic acids, which encode the targeting sequence as well as the enzyme, so that when the enzyme is expressed in the host cell, the enzyme is transported into the peroxisome (see claims 82-90). The peroxisome supplies the appropriate substrate for PHA synthesis. The enzymes leading to PHA production have specific substrates to which they bind and catalyze their formation into a product that will be specifically utilized by the next gene encoded enzyme in the pathway. Enzymes dedicated to PHA synthesis are functioning in a specific and coordinated pathway, resembling a multi-step processing unit. This is the subject of claims 91-108. The method of making the PHAs using the cells is defined by claims 121-132.

Rejection Under 35 U.S.C. § 102

Claims 82, 85, 109, 112, 114, 121, 123, 125, and 128 were rejected under 35 U.S.C. § 102(b) as being anticipated by International Symposium on Bacterial PHAs by Hahn *et al.* '96

("Hahn"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Hahn teaches the insertion of the Arg-Ala-Val-Val-Ala-Arg-Leu-COOH plant peroxisome targeting sequence at the 3' end of each of the three *Alcaligenes eutrophus* PHB pathway genes. Hahn further teaches the targeting of PHA synthase to yeast peroxisomes may be accomplished by fusing an amino-terminal targeting signal of 16 amino acids at or near the N-terminus of the PHA synthase gene. The claims are directed to a recombinant vector comprising a promoter that directs transcription of a structural nucleic acid sequence encoding a non-naturally occurring fusion protein, wherein the fusion protein comprises a peroxisome targeting protein subunit and a polyhydroxyalkanoate synthase protein subunit. The rejected claims have been amended to include all of the limitations of claims suggested to be allowed if written in independent form.

Rejection Under 35 U.S.C. § 103

Claims 82-86, 91, 92, 97-10 and 109-132 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hahn *et al., Peroxisomal Localization of PHA Synthesis in Eukaryotic Cells*, International Symposium on Bacterial Polydydroxyalkanoates '96, (abstract and poster) 16 pgs. (1996) ("Hahn"), in view of WO 92/19747 ("Bright1"); Elgersma *et al.* JBC 271, 42, p. 26375-26382 (1997) ("Elgersma"), Verleur *et al.* Eur. J. Biochem. 247, 972-980 (1997) ("Verleur"), U.S. Patent 6,146,847 to Gengenbach *et al.* ("Gengenbach"), U.S. Patent 6,258,999 to Tomes *et al.* ("Tomes"), and U.S. Patent No. 6,175,061 B1 to Bright *et al.* ("Bright2").

Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Hahn

Hahn teaches the insertion of the Arg-Ala-Val-Val-Ala-Arg-Leu-COOH plant peroxisome targeting sequence at the 3' end of each of the three *Alcaligenes eutrophus* PHB pathway genes. Hahn further teaches the targeting of PHA synthase to yeast peroxisomes may be accomplished by fusing an amino-terminal targeting signal of 16 amino acids at or near the N-terminus of the PHA synthase gene. The claims are directed to a recombinant vector comprising a promoter that directs transcription of a structural nucleic acid sequence encoding a non-naturally occurring fusion protein, wherein the fusion protein comprises a peroxisome targeting protein subunit and a polyhydroxyalkanoate synthase protein subunit. The rejected claims have been amended to include all of the limitations of claims suggested to be allowed if written in independent form.

Bright1 and Bright2

Bright is relied upon to teach the production of polyhydroxyalkanoates (3-HV, 3-HH, 3-HO, 3-HD, and 3-HB; as stated at pages 1 and 2 of Bright (WO 92/19747)). **None of Bright1 or Bright2 teach any of the specific enzymes of claim 132.**

Elgersma

Elgersma describes the targeting of a single enzyme, not involved in PHA production, using tripeptide targeting signals to the peroxisome. There is no teaching that peroxisomes

harbor appropriate substrate for PHA production, nor any teaching that would lead one to believe that there could be the coordinated enzymatic processing of substrate required to yield polymer, since neither reference discloses anything other than a single enzyme, active on a single substrate.

Hayashi

Hayashi discloses measuring protein transport into the peroxisome using tripeptide targeting signals. Hayashi does not teach the measuring of enzymatic activity in the peroxisome.

Verleur

Verleur is not concerned with an enzyme that is created with a targeting sequence for transport into the peroxisome. Verleur teaches the growth of *Saccharomyces* in specific conditions.

Gengenbach

Gengenbach teaches the use of constitutive plant promoters.

Tomes

Tomes teaches inducible plant promoters.

Summary

In order to establish a *prima facie* case of obviousness, the prior art references (when combined) must teach or suggest all of the claim limitations. None of the foregoing references, singly or in combination, teach all of the limitations now incorporated into the independent

claims. Furthermore, none of the foregoing references, singly or in combination, teach all of the enzymes cited in claim 132.

Allowance of claims 82-132 is respectfully solicited.

Respectfully submitted,

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Certificate of Facsimile Transmission

I hereby certify that this Amendment and Response to Office Action, and any documents referred to as attached therein are being facsimile transmitted on the date listed below to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Aisha Wyatt

Date: July 16, 2003

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